Docket No.: 1718-0214P
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent of:
Harmenberg, Johan et al.

U.S. Patent No.: RE39,264 E

Issued: September 5, 2006

For: Pharmaceutical Combination

REQUEST FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. §156

Mail Stop: Hatch-Waxman PTE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA
22313-1450

September 25, 2009

Sir:

Pursuant to 35 U.S.C. §165 and 37 C.F.R. §§1.710-1.791, Medivir AB. of Huddinge, Sweden (hereinafter "Applicants"), hereby request an extension of the patent term due to regulatory review for U.S. Patent No. RE39,264 E, which was granted on September 5, 2006 from a reissue application based on US patent 6,337,324. Applicants represent that they are the owners and assignees of the entire interest in and to United States Patent No. RE39,264 (Exhibit 1, hereinafter "the '264 patent") by virtue of an assignment from the inventors Johan Harmenberg and Ann Harriet Margareta Kristofferson that was recorded in the parent patent (US 6,337,324) from which instant patent reissued, according to the following chain of events: assignment from Johan Harmenberg and Ann Harriet Margareta Kristofferson to Astra Aktiebolag, recorded March 8, 1996 at Reel 008827, Frame 0772; change of name from Astra Aktiebolag to AstraZeneca AB, recorded September 6, 2001 at Reel 011933, Frame 0228; assignment from AstraZeneca AB to Medivir AB on September 6, 2001 at Reel 011965, Frame 0237 (Exhibit 2). As shown in Exhibit 2, the recordation on September 6, 2001 corrected an

invalid recording attempted on August 30, 2001 (see Reel 011938, Frame 0899). Enclosed as Exhibit 3 is a copy of the Reissue Application Declaration and Power of Attorney appointing the undersigned and Leonard R. Svensson at the undersigned's law firm as agents to transact all business with the USPTO in connection with the '264 patent.

The '264 patent matured from United States Patent Application No. 10/771,259 (the '259 application). As mentioned above, the '259 application was filed as a reissue application of US Patent 6,337,324 which had issued on January 8, 2002, and which had been designated as US Serial No.: 08/612,847 during the national phase of International Application PCT/SE96/00124 and which entered the US national phase by completing the requirements of 35 USC § 371 on March 8, 1996 (Exhibit 4).

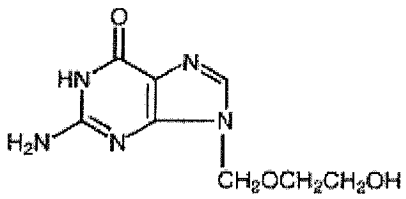
The approved product that is relevant to this application is a cream containing 5% Acyclovir and 1% Hydrocortisone for topical administration, referred to herein as "Acyclovir and Hydrocortisone Cream, 5%/1%," or "Approved Product."

The following information is submitted by Applicants, in accordance with 35 U.S.C. §156(d) and the rules for extension of patent term issued by the USPTO at 37 C.F.R. Subpart F, §§1.710 to 1.791. The following sections are numbered analogously to the format of 37 C.F.R. §1.740.

(1) Identification of the Approved Product

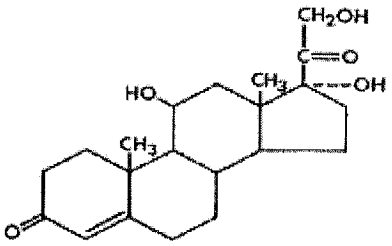
The approved product Acyclovir and Hydrocortisone Cream, 5%/1%, is a topical formulation of the active ingredients acyclovir and hydrocortisone at a synergistic concentration of 5% acyclovir and 1% hydrocortisone. Acyclovir and Hydrocortisone Cream, 5%/1%, has been approved for topical administration for the treatment of recurrent herpes labialis (cold sores).

Acyclovir is designated chemically by INN as 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-6H-purin-6-one. Additional chemical names include, but are not limited to: 2-amino-9-((2-hydroxyethoxy)methyl)-1H-purin-6(9H)-one and 9-[(2-hydroxyethyoxy)methyl]guanine. The chemical structure for acyclovir is:



Acyclovir is synthetic nucleoside analogue. The molecular weight of acyclovir is 225.21 daltons. The empirical formula is $C_8H_{11}N_5O_3$. The maximum solubility of acyclovir in water at 37°C is 2.5 mg/mL. The pKa of acyclovir is 2.27 and 9.25.

Hydrocortisone is designated chemically by INN as pregn-4-ene-3, 20-dione, 11, 17, 21-trihydroxy-(11(beta))-. Additional chemical names include, but are not limited to: (11β)-11,17,21-trihydroxy-pregn-4-ene-3,20-dione and 4-pregnene-11β,17α,21-triol-3,20-dione. The chemical structure for hydrocortisone is:



Hydrocortisone is a glucocorticoid, specifically an anti-inflammatory corticosteroid. The molecular weight of hydrocortisone is 362.47 daltons. The empirical formula is $C_{21}H_{30}O_5$.

Acyclovir and Hydrocortisone Cream, 5%/1%, is supplied as a topical cream, and contains as the active ingredient a synergistic combination of 5% acyclovir, a synthetic nucleoside analogue active against herpes viruses, and 1% hydrocortisone. It also contains the following inactive ingredients: cetostearyl alcohol, mineral oil, Poloxamer 188, propylene glycol, isopropyl myristate, sodium lauryl sulfate, white petrolatum, citric acid, sodium hydroxide and water.

Sodium hydroxide or hydrochloric acid may be added to adjust the pH to approximately pH 5.

(2) Identification of the Federal Statute under which Regulatory Review Occurred

The approved product is a drug product and the submission was approved under Section 505(b) of the Federal Food, Drug, and Cosmetic Act ("FFDCA") (21 U.S.C. § 355(b)).

(3) The Date of Permission for Commercial Marketing

The Approved Product received permission for commercial marketing or use by the Food and Drug Administration ("FDA") pursuant to Section 505(b) of the FFDCA (21 U.S.C. § 355(c)) in a letter dated July 31, 2009 containing the electronic signatures of Debra Birnkrant, M.D., Direction of the Division of Antiviral Products, Office of Antimicrobial Products, Center for Drug Evaluation and Research and Jeffrey S. Murray. A copy of the FDA approval letter is attached as Exhibit 5.

(4) Active Ingredient Statement

Applicant states that the active ingredient of the Approved Product is a synergistic combination of 5% acyclovir and 1% hydrocortisone. Please note that the synergistic combination of 5% acyclovir and 1% hydrocortisone is a different active ingredient from 5% acyclovir, which is marketed as Zovirax® (NDA 21-478). The synergistic combination of 5% acyclovir and 1% hydrocortisone is also a different active ingredient from 1% hydrocortisone.

(5) Statement of Timely Filing

This application is timely filed, pursuant to 35 U.S.C. § 156(d)(1), within the permitted sixty-day (60-day) period that began on July 31, 2009 when the product received permission under 21 U.S.C. § 355(b) and that will expire on September 29, 2009.

(6) Identification of Patent for which Extension is Sought

The expiration date of U.S. Patent No. RE39,264 ("the '264 patent") is February 2, 2016 based on the following:

The patent application that issued as the '264 patent, U.S. Application No. 10/771,259, issued on September 5, 2006 as a Reissued Patent of US 6,337,324 ("the parent '324 patent").

The parent '324 patent issued from an application (08/612,847) that was the national stage filing of PCT Application No. PCT/SE96/00124, filed on February 2, 1996 (Exhibit 4). Thus, the earliest filing date for the '264 patent for purposes of patent term calculation is February 2, 1996, and 20 years from this date is February 2, 2016.

The '264 patent is subject to a terminal disclaimer (Exhibit 7), disclaiming any patent term beyond the expiration of the full term of US Patent No. 6,068,860 ('860; Exhibit 6). The expiration date of the '860 patent is February 2, 2016, which is 20 years from its PCT international filing date, of February 2, 2016. Consequently, the terminal disclaimer has no effect on the patent term and the expiration date of the '264 patent is February 2, 2016.

Johan Harmenberg and Ann Harriet Margareta Kristofferson are named as inventors.

(7) Patent Copy

A complete copy of U.S. Patent No. RE39,264 E is attached as Exhibit 1.

(8) Post-Issuance Activity Statement

United States Patent No. RE39,264 E is subject to a Terminal Disclaimer (Exhibit 7).

United States Patent No. RE39,264 E has not been re-examined, nor has the parent '324 patent, therefore no reexamination certificate has been issued.

No certificates of correction have been filed for U.S. Patent No. RE39,264 E, however a certificate of correction was filed for the parent '324 patent (Exhibit 12).

The first maintenance fee (i.e. the 4th year) for the parent '324 patent (i.e. U.S. Patent No. 6,337,324) was paid June 9, 2005, as shown by the Patent Bibliographic Data Sheet and the USPTO Maintenance Fee Statement for the parent '324 patent, both dated September 25, 2009, and both found in Exhibit 13.

The first maintenance fee (i.e. the 8th year) for U.S. Patent No. RE39,264 E was paid June 15, 2009, as shown by the Patent Bibliographic Data Sheet and the USPTO Maintenance Fee Statement for this patent, both dated September 15, 2009, and both found in Exhibit 8. The next maintenance fee is not yet due. The payment window for the next maintenance fee (12th year fee) does not open until January 8, 2013. Accordingly, there are no unpaid maintenance fees for this patent.

(9) Statement Showing How the Claims of the Patent for which Extension is Sought Cover the Approved Product

U.S. Patent No. RE39,264 E claims the Approved Product. Specifically, compound claims 2, 4, 7 and 13-16 read on the Approved Product as do method claims 18, 20, 23, 24, 25, 27-31 and 33-37. Pursuant to 37 C.F.R. § 1.740(a)(9), a showing which demonstrates the manner in which at least one claim reads on the approved product is set forth herein below.

CLAIM	ELEMENTS
2. A pharmaceutical composition for topical administration *to treat recurrent herpes infections* comprising, as *sole active drug*	The active ingredient (also commonly referred to as the "effective ingredient") of Acyclovir and Hydrocortisone Cream, 5%/1% is a

substances, a [synergistic] combination of a*n* [topically acceptable] antiviral [substance] *ingredient* selected from the group consisting of *foscarnet*, acyclovir, [cidofovir, desciclovir, famciclovir, ganciclovir, lobucavir,] penciclovir, [PMEA, valacyclovir, 2242, PAA, PFA] and 9-[4-hydroxy-2-(hydroxymethyl)butyl]guanine (H2G), or [an ester,] a salt [or solvate] thereof and an anti-inflammatory glucocorticoid *ingredient selected from the group consisting of hydrocortisone and esters thereof,* in a pharmaceutically acceptable carrier, *wherein said combination of antiviral and glucocorticoid is more effective in treating said herpes infections than either ingredient alone.*	synergistic combination of the antiviral acyclovir and anti-inflammatory glucocorticoid hydrocortisone. The Acyclovir and Hydrocortisone Cream, 5%/1% is significantly more efficacious (i.e. has a synergistic effect) than either acyclovir or hydrocortisone alone (see Exhibit 9)
18. A method for [the prophylaxis and/or treatment of] *treating recurrent* herpesvirus infections of the skin or mucous membranes in mammals *having or identified as being at risk of developing said infections* comprising topically administ[ration]*ring thereto, as sole active drug substances and* in combination or in sequence, [of a therapeutically synergistic dose of] [a topically acceptable] *an* antiviral *substance* ingredient selected from the group consisting of *foscarnet*, acyclovir, [cidofovir, desiciclovir, famciclovir, ganciclovir,	As discussed above, Acyclovir and Hydrocortisone Cream, 5%/1% is a pharmaceutical composition containing a synergistic combination of the antiviral acyclovir and anti-inflammatory glucocorticoid hydrocortisone as the active ingredient. The Acyclovir and Hydrocortisone Cream, 5%/1% is significantly more efficacious (i.e. has a synergistic effect) than either acyclovir or hydrocortisone alone (see Exhibit 9) and is used to treat recurrent herpesvirus infections.

lobucovir,] penciclovir, [PMEA, valacyclovir, 2242, PAA,] and *9-[4-hydroxy-2-(hydroxymethyl)butyl]guanine* (H2G), or [an ester,] *a* salt [or solvate] thereof and an anitiinflammatory glucocorticoid i*ngredient selected from the group consisting of hydrocortisone and esters thereof,* in a pharmaceutically acceptable carrier, *wherein said antiviral and glucocorticoid are more effective in treating said herpesvirus infections than either ingredient alone.*	

(10) Statement of the Relevant Dates to Determine the Regulatory Review Period

The relevant dates and information pursuant to 35 U.S.C. §156(g) to enable the Secretary of Health and Human Resources to determine the applicable regulatory review period are as follows:

(i)The patent for which extension of term is sought claims a human drug product.

(A) An original Investigational New Drug Application ("IND") was filed on June 18, 1999, and assigned IND No. 58,500. Applicants received a letter from the FDA stating that the IND application was received on June 21, 1999. A copy of this letter, dated July 9, 1999, which acknowledged receipt of the IND is attached as Exhibit 10. Accordingly, IND No. 58,500 became effective 30 days from June 21, 1999, which is July 21, 1999.

(B) A New Drug Application ("NDA") was submitted on September 30, 2008 and was acknowledged as received on October 1, 2008 in a letter from the FDA dated July 31, 2009 (Exhibit 5). This letter indicated that the NDA was assigned number 22-436. Accordingly, the NDA was initially submitted on October 1, 2008.

(C) The NDA 22-436 was approved on July 31, 2009 (Exhibit 5).

(11) Brief Description of Activities Undertaken During the Regulatory Review Period

In accordance with 37 C.F.R. § 1.740(a)(11), enclosed as Exhibit 11 is a chronology of the major communications between the FDA and the Marketing Applicant in IND No. 58,500 and NDA No. 22-436 during the applicable regulatory review period.

(12) Opinion of Eligibility for Extension

Applicants are of the opinion that U.S. Patent No. RE39,264 E is eligible for extension under 35 U.S.C. §156 and 37 C.F.R. §1.720 because it satisfies all of the requirements for such extension as follows:

(a) 35 U.S.C. §156(a) and 37 C.F.R. §1.720(a)

U.S. Patent No. RE39,264 E claims, a synergistic combination of 5% acyclovir and 1% hydrocortisone, the active ingredient of a human drug product, pharmaceutical compositions containing the active ingredient and a method of using it as discussed above in section (9).

(b) 35 U.S.C. §156(a)(1) and 37 C.F.R. §1.720(g)

The term of U.S. Patent No. RE39,264 E is currently set to expire on February 2, 2016 and, therefore, has not expired before the submission of this application.

(c) 35 U.S.C. §156(a)(2) and 37 C.F.R. §1.720(b)

The term of U.S. Patent No. RE39,264 E has never been extended.

(d) 35 U.S.C. §156(a)(3) and 37 C.F.R. §1.720(c)

The application for extension of the term of U.S. Patent No. RE39,264 E is submitted by the authorized attorney of the owners of record thereof in accordance with the requirements of 35 U.S.C. §156(d) and 37 C.F.R. §1.740.

(e) 35 U.S.C. §156(a)(4) and 37 C.F.R. §1.720(d)

The approved product, Acyclovir and Hydrocortisone Cream, 5%/1%, has been subjected to a regulatory review period before its commercial marketing or use, as evidenced by the approval letter of July 31, 2009 from the FDA to Medivir, AB. (Exhibit 5).

(f) 37 C.F.R. §1.720(h)

No other patent has been extended for the same regulatory review period for the approved product, Acyclovir and Hydrocortisone Cream, 5%/1%.

(g) 35 U.S.C. §156(a)(5)(A) and 37 C.F.R. §1.720(e)(1)

The permission for the commercial marketing or use of the approved product, Acyclovir and Hydrocortisone Cream, 5%/1%, is the first received permission for commercial marketing or use of Acyclovir and Hydrocortisone Cream, 5%/1%, under the provision of law under which the applicable regulatory review occurred. (See also section (4) above).

Length of Extension Claimed Under 37 C.F.R. §1.740(a)(12) and Determination of Length of Extension Under 37 C.F.R. § 1.775

The length of extension of the patent term of U.S. Patent No. RE39,264 E, now expiring on February 2, 2016, requested by Applicants is 1533 days, which length was calculated in accordance with 37 C.F.R. §1.775 as follows:

(a) The regulatory review period under 35 U.S.C. §156(g)(1)(B) began on July 21, 1999 (the effective date of the IND No. 58,500) and ended on July 31, 2009 (NDA approval letter date), amounting to a total of 3664 days which is the sum of (i) and (ii) below:

(i) The period of review under 35 U.S.C. §156(g)(1)(B)(i), the "Testing Period," began on July 21,1999 and ended on October 1, 2008 with submission of the NDA No. 22-436 which is 3361 days;

(ii) The period for review under 35 U.S.C. §156(g)(1)(B)(ii), the "Application Period," began on October 1, 2008 and ended on July 31, 2009, which is 303 days;

(b) The regulatory review period upon which the period for extension is calculated is the entire regulatory review period as described in subparagraph (a) immediately above (3664 days) less:

(i) The number of days in the regulatory review period which were on or before the date on which the patent issued (January 8, 2002), i.e., 902 days, and

(ii) The number of days during which the Applicants did not act with due diligence, i.e., 0 days, and

(iii) One-half of the number of days remaining in the period in subparagraph (a)(i) immediately above after subtracting the number of days in the subparagraphs immediately above denoted as (b)(i) and (b)(ii), which is one-half of (3661 - [902 + 0]) or 1229 days;

Which results in a period of 3664 - [902 + 0 + 1229 days] = 1533 days.

(c) The number of days as determined in subparagraph (b) immediately above, when added to the original term (February 2, 2016), would result in the date of April 14, 2020.

(d) Fourteen (14) years when added to the date of the NDA Approval Letter (July 31, 2009) would result in the date of July 31, 2023.

(e) The earlier date as determined by the subparagraphs immediately above denoted as (c) and (d) is April 14, 2020.

(f) Since the original patent was issued after September 24, 1984, the extension otherwise obtainable is limited to not more than five (5) years. Five years, when added to the original expiration of U.S. Patent No. RE39,264 E (February 2, 2016), results in the date February 2, 2021.

(g) The earlier date as determined in the subparagraphs immediately above denoted as (e) and (f) is April 14, 2020.

Conclusion: Accordingly, U.S. Patent No. RE39,264 E is eligible for a patent term extension of 1533 days.

(13) Duty of Disclosure Acknowledgement Under 37 C.F.R. §1.740(a)(13)

Applicants acknowledge a duty to disclose to the Commissioner of Patent and Trademarks and the Secretary of Health and Human Services any information which is material to the determination of entitlement to the extension sought.

(14) Fee Charge

The prescribed fee of $1,120 under 37 C.F. R. § 1.20(j)(1) for receiving and acting upon this application is to be charged to Applicant's Deposit Account No. 02-2448 as authorized in the attached transmittal letter, submitted in triplicate. The Director is hereby authorized to charge our deposit account No. 02-2448 under docket number 1718-0214P for any deficiency in the fees filed, asserted to be filed, or which should have been filed herewith, or with any paper herein after filed in the application/patent by this firm.

(15) Correspondence Address Required by 37 C.F.R. §1.740(a)(15)

All correspondence relating to this application for patent term extension should be addressed to:

Susan W. Gorman
Birch, Stewart, Kolasch & Birch, LLP
P.O. Box 747
Falls Church, VA 22040

(16) Certification Under 37 C.F.R. §1.740(b)

The undersigned hereby certifies that the instant application, including its attachments and supporting papers, is being submitted as one original and two copies thereof in accordance with 37 C.F.R. §1.740(b).

Dated: September 25, 2009

Respectfully submitted,

By _____
Susan W. Gorman
Registration No.: 47,604
BIRCH, STEWART, KOLASCH & BIRCH, LLP
P.O. Box 747
Falls Church, VA 22040-0747
(858) 792-8855
Attorney for Applicants